



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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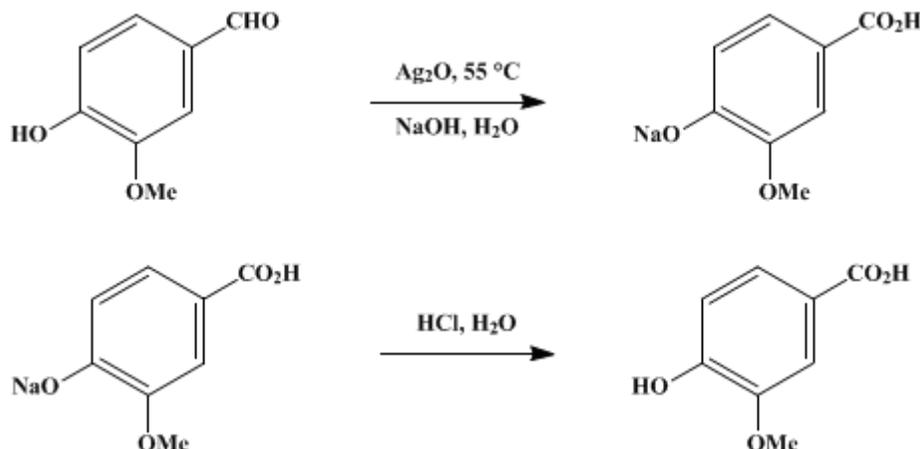
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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VANILLIC ACID

[I. SILVER OXIDE METHOD]



Submitted by Irwin A. Pearl¹

Checked by R. L. Shriner and Calvin N. Wolf.

1. Procedure

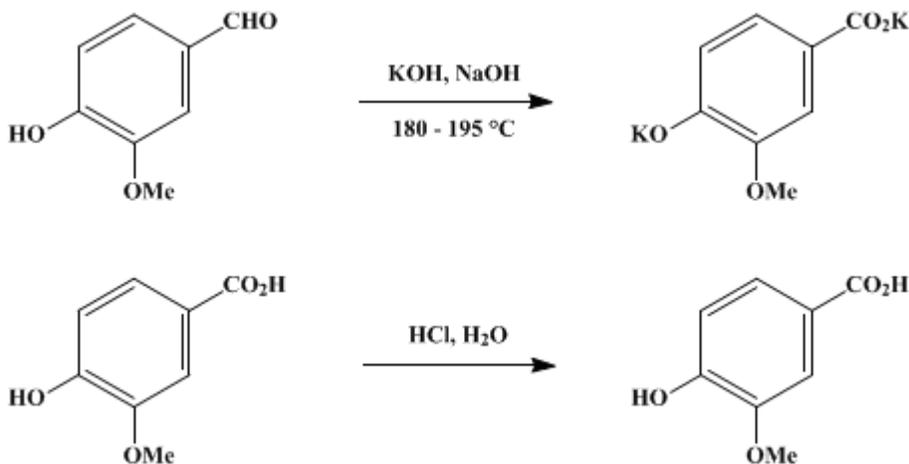
A solution of 170 g. (1.0 mole) of silver nitrate in 1 l. of water in a 2-l. beaker is treated, with stirring, with a solution of 44 g. (1.07 moles) of 97% sodium hydroxide in 400 ml. of water (Note 1). The mixture is stirred for 5 minutes, and the silver oxide is collected on an 11-cm. Büchner funnel with suction and washed free of nitrates with water (Note 2). The wet, freshly precipitated silver oxide is transferred to a 4-l. beaker (Note 1), covered with 2 l. of water, and treated with 200 g. (4.85 moles) of 97% sodium hydroxide pellets with vigorous stirring. If the temperature of the mixture at this point is below 55° , the mixture is warmed to $55\text{--}60^\circ$. With continued stirring at $55\text{--}60^\circ$ (Note 3), 152 g. (1.0 mole) of vanillin (Note 4) is added; the reaction begins after a few minutes. The silver oxide is transformed to fluffy metallic silver, and considerable heat is evolved. Stirring is continued for 10 minutes, the mixture is filtered, and the precipitated silver is washed with 100 ml. of hot water. A rapid stream of sulfur dioxide gas (Note 5) is passed into the combined filtrate and washings for 2 minutes, and the resulting solution is poured into 1.1 l. of 1:1 hydrochloric acid with vigorous stirring. The resulting mixture, which should be acid to Congo red, is cooled to $15\text{--}20^\circ$. The vanillic acid is collected on a Büchner funnel, pressed to remove the mother liquor, washed with 150 ml. of ice water (Note 6), sucked as dry as possible, and air-dried. The yield is 140–160 g. (83–95%) of white needles melting at $209\text{--}210^\circ$. This product is pure enough for most purposes, but it may be purified by recrystallization from water containing a little sulfur dioxide, 1.2 l. of water being used per 100 g. of product. Pure white needles melting at $210\text{--}211^\circ$ are obtained with a recovery of 90–97%.

2. Notes

1. This reaction should be performed in glass apparatus with a glass stirrer. If stainless steel is employed, the resulting vanillic acid may be dark in color.
2. The presence of nitrates in the solution will cause the formation of nitro acids when the final acidification takes place.
3. Fifty to fifty-five degrees was found to be the critical temperature for this reaction. If the reactants are mixed cold, heat must be applied to raise the temperature above 50° , at which point the reaction begins. Mixing of the reactants at temperatures much higher than 60° results in a violent reaction.
4. Commercial U.S.P. vanillin is satisfactory.
5. The treatment with sulfur dioxide prevents the product from becoming tan in color.
6. Extraction of the combined filtrate and washings with three 200-ml. portions of ether, followed by

removal of the ether by distillation, yields an additional 4–20 g. of product melting at 206–208°. It may be purified by recrystallization from water containing a little sulfur dioxide to give white needles melting at 209–210°.

[II. CAUSTIC FUSION METHOD]



Submitted by Irwin A. Pearl¹

Checked by R. L. Shriner and Robert C. Johnson.

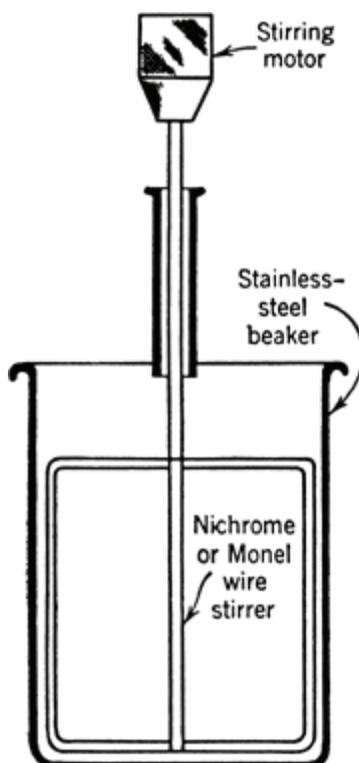
1. Procedure

In a stainless-steel beaker of approximately 2-l. capacity (120 mm. by 165 mm.) equipped with an efficient mechanical Nichrome or Monel stirrer (Note 1) and heated by an electric hot plate are placed 178 g. (4.3 moles) of 97% sodium hydroxide pellets, 178 g. (2.7 moles) of 85% potassium hydroxide pellets (Note 2), and 50 ml. of water. The mixture is stirred and heated to 160°, at which temperature the hot plate is turned off. Twenty-five grams of vanillin is added. The temperature drops somewhat, and after a very short time a vigorous reaction begins which raises the temperature to 180–195°. An additional 127 g. (total of 1.0 mole) of vanillin is gradually added to the reaction mixture during a period of 10–12 minutes at a rate sufficient to maintain the reaction temperature (Note 3). After all the vanillin has been added, stirring is continued for 5 minutes. The hot plate is removed, and the mixture is allowed to cool with stirring. When the mixture cools to about 150–160°, 1 l. of water is added and the mixture is stirred until all the fusion mixture is dissolved. The solution is transferred to a 4-l. beaker, 500 ml. of water being used to rinse the stirrer and metal beaker. Sulfur dioxide gas is introduced for 1 minute (Note 4), and the reaction mixture is cooled to room temperature. The mixture is acidified with about 1.2 l. of 6*N* hydrochloric acid using Congo red as the indicator and keeping the mixture cool during addition of the acid by stirring and cooling in an ice bath. The mixture is cooled, and the light-tan precipitate is filtered, washed with 150 ml. of ice water, and dried. The yield of vanillic acid melting at 206–208° is 150–160 g. (89–95%) (Note 5). The product can be recrystallized from water, using 1.2 l. per 100 g. of vanillic acid. A 90–97% recovery of nearly white vanillic acid melting at 209–210° is obtained.

2. Notes

1. An efficient stirrer can be made from No. 8 Nichrome or Monel metal wire in a rectangular shape of dimensions such that it is about two-thirds the height of the beaker and has a clearance of 1–2 mm. with the sides of the beaker (Fig. 18). A rigid form is maintained by spot-welding the crossed wires. The metal beaker must be firmly clamped. It is important that there be effective stirring throughout all the reaction mixture in order to prevent caking, excessive local temperature rises, and foaming.

Fig. 18. Apparatus for caustic fusion of vanillin.



2. The exact proportion of **sodium hydroxide** to **potassium hydroxide** is not critical as long as the total amount of alkali is more than 7 moles. Alkali mixtures containing more than 70% **sodium hydroxide** are not desirable because they are not as fluid as other mixtures.
3. The temperature of the mixture should not be allowed to rise much above 200° for any length of time because traces of **protocatechuic acid** will be formed and contaminate the **vanillic acid**.
4. The **sulfur dioxide** treatment prevents the product from becoming tan in color.
5. An additional few per cent may be obtained by **ether** extraction of the filtrate.

3. Discussion

Vanillic acid has been prepared from **vanillin** in small amounts by action of moist air,² exposure to sunlight and **nitrobenzene**,³ reaction with soil bacteria,⁴ **ozone**,⁵ and by caustic fusion.^{6,7} High yields of **vanillic acid** have been obtained from **vanillin** by controlled caustic fusion,⁸ oxidation with **silver oxide**,^{9,10} **mercuric oxide**,¹¹ and **gold oxide**,¹¹ and by the Cannizzaro reaction of **vanillin** in the presence of a **silver** catalyst.¹² **Vanillic acid** has been prepared indirectly from **vanillin** by the hydrolysis of **acetylvanillic acid** prepared by oxidation with **peracetic acid** of **acetylvanillin**,¹³ by the hydrolysis of **acetovanillonitrile** prepared by the reaction of **vanillin oxime** with **acetic anhydride**,¹⁴ and by the action of hydrazoic acid on **vanillin**, followed by hydrolysis of the intermediate **4-hydroxy-3-methoxybenzonitrile**.¹⁵ The procedures described are essentially those reported by Pearl.^{8,9,16}

References and Notes

1. Institute of Paper Chemistry, Appleton, Wisconsin.
2. Tiemann, *Ber.*, **8**, 1134 (1875).
3. Ciamician and Silber, *Ber.*, **38**, 3821 (1905).
4. Robbins and Lathrop, *Soil Sci.*, **7**, 475 (1919).
5. Dorland and Hibbert, *Can. J. Research*, **18B**, 33 (1940).
6. Lock, *Ber.*, **62**, 1187 (1929).
7. Sabalitschka and Tietz, *Arch. Pharm.*, **269**, 545 (1931).
8. Pearl, *J. Am. Chem. Soc.*, **68**, 2180 (1946).

9. Pearl, *J. Am. Chem. Soc.*, **68**, 429 (1946).
 10. Pearl, *J. Am. Chem. Soc.*, **68**, 1100 (1946).
 11. Pearl, *J. Am. Chem. Soc.*, **67**, 1628 (1945).
 12. Pearl, *J. Org. Chem.*, **12**, 79 (1947).
 13. Böeseken and Greup, *Rec. trav. chim.*, **58**, 528 (1939).
 14. Raiford and Potter, *J. Am. Chem. Soc.*, **55**, 1682 (1933).
 15. Schuerch, *J. Am. Chem. Soc.*, **70**, 2293 (1948).
 16. Pearl and Beyer, *Ind. Eng. Chem.*, **42**, 376 (1950); **44**, 2893 (1952).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

hydrazoic acid

hydrochloric acid (7647-01-0)

ether (60-29-7)

acetic anhydride (108-24-7)

sodium hydroxide (1310-73-2)

silver oxide (20667-12-3)

silver nitrate (7761-88-8)

sulfur dioxide (7446-09-5)

mercuric oxide (21908-53-2)

potassium hydroxide (1310-58-3)

Nitrobenzene (98-95-3)

silver (7440-22-4)

ozone (10028-15-6)

vanillin (121-33-5)

protocatechuic acid (99-50-3)

peracetic acid (79-21-0)

Vanillic acid (121-34-6)

gold oxide

acetyl-vanillic acid

acetyl-vanillin (881-68-5)

acetovanillonitrile

vanillin oxime

4-hydroxy-3-methoxybenzonitrile (4421-08-3)

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